

IN THE SPECIFICATION

Please amend the specification by inserting the following replacement paragraphs:

Please replace the paragraph at page 21, line 34 to page 22, line 12 with the following:

--The toxin is dissolved at an adequate concentration in a buffer. While the pH is adjusted to a pH at which toxic activity is generally lost, including an acidic pH (for example, pH 2 to 4) or alkaline pH (for example, pH 8 to 11), the solution is incubated at an adequate temperature. Alternatively, the solution is incubated at a temperature at which the toxic activity is generally lost (for example, at a temperature of 40°C or higher). Otherwise, the toxin is sonicated at an adequate wavelength, or irradiated with electromagnetic wave. The residual toxic activity of the sample is assayed before, during and after the treatment. If desired, the attenuated toxin is re-incubated at an adequate temperature, for example, at 37°C, to confirm that the attenuated toxin does not revert to toxicity. If the activity of enhancing immunity is confirmed to be sufficiently high, then the preparation of attenuated toxin is completed. The chemical and physical treatments for attenuation can be properly combined.--

Please replace the paragraph at page 33, line 28 to page 34, line 10 with the following:

--A cholera toxin-producing bacterium (*Vibrio cholera*; Inaba type 569B strain) was cultured in a semi-synthetic casamino acid medium (liquid medium containing glucose) designed by Finkelstein et al., at 30°C for 20 hours. After the culture was completed, the culture supernatant was subjected to ultrafiltration, using a filter having pores that the cholera toxin molecule (molecular weight; 86,000 Da) could freely go through. A small amount of aluminum hydroxide gel was added to the filtrate. The gel was allowed to adsorb the toxin and then was collected by centrifugation. The toxin was eluted from the gel with 10% phosphate-10% citrate (pH 7.6), while incubating at 30 to 35°C. The eluted liquid was dialyzed against an aqueous solution containing 0.1 M citrate. Then, the solution was loaded onto a column of DEAE-Sephadex and the toxin was eluted with phosphate buffer containing 0.1 to 0.2 M saline (hereafter abbreviated as PBS). Subsequently, the sample was loaded onto a column of Sephadex G-75 and the toxin was eluted with PBS. The resulting sample was subjected to gel electrophoresis. The presence of the cholera toxin only was detected as a single band. The purity was about 95%. The yield was 250 mg/100L culture broth.--

Please replace the paragraph at page 37, line 23 to page 38, line 6 with the following:

--A variety of attenuated cholera toxins, of which residual toxic activities were all less than one-two thousandth of that of the natural one, were used as the adjuvants. The same experiment as in Example 2 was repeated several times to assay the titer of anti-HA-IgA in the nasal washes and titer of IgG antibody in the blood of mice. The antibody titers determined in each assay were converted to relative values to those observed when the same amounts of natural cholera toxin were used as positive controls. The relative value is indicated as the ordinate axis and the attenuation rate of the toxin (relative residual activity to the natural one) was indicated as the abscissa axis (Figure 4). It is obvious that the majority of attenuated toxins, of which residual toxic activities are less than one-two thousandth that of the natural one (one-two thousandth = $4^{-5.46}$), exhibit high levels of antibody production-enhancing activity comparable to that of the same amount of natural cholera toxin. In particular, it was verified that the attenuated toxins, of which residual toxic activities are reduced to less than one-two thousandth that of the natural one, show on intranasal administration equal or higher efficacy as compared to that of original toxin in regard to the enhancement of antigen-specific mucosal IgA formation.--

Please replace the paragraph at page 39, lines 11 to 14 with the following:

The result shows that both adjuvants of the invention, whether the natural toxin or the recombinant mutant toxin, exhibit activity of enhancing immunity of influenza vaccine administered by the intranasal vaccination route.